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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,047	11/08/2005	Roger Michael Lane	4-32609A	7567

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ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
POHNERT, STEVEN C	
ART UNIT	**PAPER NUMBER**
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,047	LANE, ROGER MICHAEL	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-20,22-29 and 31-42* is/are pending in the application.

4a) Of the above claim(s) *33-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-20,22-29,31 and 32* is/are rejected.

7)☒ Claim(s) *2,9,14,20,22 and 29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *118/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I, claims 1-9, 11-20, 22-29 and 3-32 in the reply filed on 3/6/2007 is acknowledged.

2. Claims 33-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/6/2007.

Information Disclosure Statement

3. The information disclosure statement filed 11/8/2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Copies of non-patent literature and foreign patents marked out have not been provided and thus are not considered.

Claim Objections

4. Claims 2, 9, 14, 20, 22, 29 are objected to because of the following informalities: Claims 2, 9, 14, 20, 29 refer to ChEI selected from table 1. The claim refers to tables. MPEP 2173.05(s) states:

> Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience."

This can easily be overcome by amending the claims to recite the ChEI recited in

the tables.

Claim 22 is dependent from claim 21, which has been canceled. For art purposes claim 22 will be interpreted as being dependent to claim 20, as claim 21 was dependent from claim 20.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-28 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors have been described by the court in re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in the Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction

or guidance presented, (3) the presence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and the breadth of the claims:

The claims refer to the APOE-ε4 allele. The art refers to APOE-ε4 as the protein encoded by the APOE4 allele, thus as the claims are drawn to nucleotides the allele of interest will be referred to as APOE4 throughout this office action.

Claims 25-27 and 31 are drawn to a method of determining responsiveness to a individual with dementia based on APOE4 genotype, wherein the presence of no APOE4 alleles is placed in a non-responder group. The claims further draw the claims to the dementia being Alzheimer's disease (AD) and treatment with rivastigmine.

Claim 28 is a method drawn to the prediction of level of care of a patient with dementia based on APOE4 genotype. The claim is broadly drawn to predicting the future based on a genotype. The claim is drawn to the continued deterioration of a patient without the APOE4 allele.

The amount of direction or guidance and the Presence and absence of working examples.

The specification teaches a phase III clinical trial of 26 weeks as to the effect of rivastigmine on patients with probable AD (see page 25, last paragraph). The specification teaches there was no difference in the response to treatment with >= 6mg/day of rivastigmine in patients with an APOE4 (e4 allele) compared to those without (see table 7)(p=0.1172) as measured by non-deterioration in the ADAS-Cog

score. The specification further asserts on page 27 2nd full paragraph that there are higher rates of response in patients that are APOE4 carriers and asserts a p=0.00000175. However table 8 appears to teach that 26 of 54 patients with APOE4 allele were observed to have a 4 point improvement, while 26 of 54 patients without the APOE4 allele also had a 4 point improvement. It does not appear that the data supports the assertion that there is a statistical significant difference between groups with the allele of interest compared to those without. It furthers appears that the teachings of Table 9, that there is a significant difference between APOE4 carriers treated with >= 6mg/day of rivastigmine (p=0.0000151), but non-carriers. The specification teaches that 20 patients with no APOE4 allele did not deteriorate in response to treatment with rivastigmine, suggesting that the presence of APOE4 by itself is not predictably associated with response to rivastigmine (see table 7). The specification further teaches that genotype effect of the rivastigmine treatment is dependent on dosage (see table 10). The specification thus teaches that the absence of the APOE4 genotype is not predictably associated with continued deterioration. The specification further teaches that the response to rivastigmine is not predictably associated with improved ADAS-cog score in doses less than 6mg/day.

The specification does not provide any teaching as to the level of care required based upon the APOE4 genotype.

The level of skill in the art:

The level of skill in the art is deemed to be high.

Quantity of experimentation necessary:

The claims assert the APOE ε4 alleles are good responders.

In order to practice the invention as claimed, one would first have to establish that a predicative relationship exists between the APOE4 genotype and response to treatment for dementia. Further one of skill in the art would further have to determine if a predictive relationship exists between the APOE4 genotype and the future level of care required. Experimentation would be replete with unpredictable trial and error analysis because the specification appears to have conflicting teaching to the effect of the APOE4 genotype and responsiveness to treatment with rivastigmine. In table 7 the specification teaches the genotypes ε4are not statically correlated with the treatment response placebo, < 6mg/day or 6 mg/day or more rivastigmine. The specification further provides no teachings to support that the APOE4 genotype plays any role in predicting the near future level of care required. The specification actually teaches that 20 of 41 patients without the APOE4 allele did respond to treatment as measured by lack of deterioration. Thus the absence of the APOE4 gene is not predictably associated with continued deterioration. One of skill in the art would have to recruit an enormous population of dementia patients and determine if the APOE4 genotype is associated with increased responsiveness to rivastigmine treatment or level of care required.

Further claim 28, appears to be claiming the ability to predict the future based on genotype.

Due to the scope of the claims, one of skill in the art would be required to further undertake extensive trial and error experimentation.

Therefore, in light of the breadth of the claims, the lack of guidance in the specification, the high level of unpredictability in the associated technology, the nature of the invention, the negative teachings in the art, and the quantity of unpredictable experimentation necessary to practice the claimed invention, it would require undue experimentation to practice the invention as claimed.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-9, 11-20, 23-30, 31, 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 are indefinite because it lacks a positive active step relating back to the preamble. The preamble recites a method of prevention deterioration of cognitive function in a patient, however the last positive active step is drawn to treating a patient with ChEI depending on APOE genotype. Therefore it is unclear as to whether the method is drawn to prevention deterioration of cognitive function in a patient or treating a patient with ChEI depending on APOE genotype.

Claims 7-9, 11 are indefinite because it lacks a positive active step relating back to the preamble. The preamble recites a method of prevent worsening of behavior problems in a patient, however the last positive active step is drawn to treating a patient with ChEI depending on APOE genotype. Therefore it is unclear as to whether the method is drawn to prevent worsening of behavior problems in a patient or treating a patient with ChEI depending on APOE genotype.

Claims 12-18 are indefinite because it lacks a positive active step relating back to the preamble. The preamble recites a method to improve cognitive impairment in a patient, however the last positive active step is drawn to treating a patient with ChEI depending on APOE genotype. Therefore it is unclear as to whether the method is drawn to improve cognitive impairment in a patient or treating a patient with ChEI depending on APOE genotype.

Claims 19-20, 23-24, 32 are indefinite because it lacks a positive active step relating back to the preamble. The preamble recites a method of prevent worsening of behavior problems in a patient, however the last positive active step is drawn to treating a patient with ChEI depending on APOE genotype. Therefore it is unclear as to whether the method is drawn to prevent worsening of behavior problems in a patient or treating a patient with ChEI depending on APOE genotype.

Claims 25-27, 29, 31 are indefinite because it lacks a positive active step relating back to the preamble. The preamble recites a method of determining responsiveness of an individual with dementia to treatment with ChEI, however the last positive active step is drawn to placing the patients with the no APOE4 alleles in the poor responder group. Therefore it is unclear as to whether the method is drawn to determining responsiveness of an individual with dementia to treatment with ChEI or placing the patients with the no APOE4 alleles in the poor responder group.

Claim 28 is indefinite because it lacks a positive active step relating back to the preamble. The preamble recites a method of predicting the level of care for a patient with dementia, however the last positive active step is determining the genotype of

APOE. Therefore it is unclear as to whether the method is drawn to predicting the level of care for a patient with dementia or last positive active step is determining the genotype of APOE.

8. The term "worsening" in claims 7-9 is a relative term, which renders the claim indefinite. The term "worsening" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

9. The term "improve" in claims 12-18 is a relative term which renders the claim indefinite. The term "improve" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. This rejection can easily be overcome by amending the claim to recite, "a 4 point improvement in ADAS-Cog score.

10. The term "good responder" and "poor responder" in claims 25-27, 31 are a relative term, which renders the claim indefinite. The term "good responder" and "poor responder" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. This rejection can easily be overcome by amending the claim to recite, "a 4 point improvement in ADAS-Cog score."

11. Claim 28 is indefinite in that it recites, " in the near future." It is unclear the metes and bounds of the "in the near future." Is the near future 1-second, a day, a month, a year, 10 years, etc?

12. Claim 28 is indefinite it that it recites in quotations "remain stable or improve" and "continued deterioration". It is unclear if the quotations around these phrases reflect a limitation of the claim.

Claim Rejections - 35 USC § 101

13. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 25- 29, 31-32 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims 25-27, 29 and 31-32 are drawn to methods of determining responsiveness of an individual to treatment with a ChEI drug, by determining the genotype of the APOE gene and assigning an individual to a group based on the genotype. The methods as claimed, do not produce any physical transformation or produce a tangible result. The claims as written, encompass mere mental steps i.e. determining a genotype for future use and assigning to groups. The step of determining the genotype of two copies of APOE gene and assigning to a group, does not produce any physical transformation or produce a tangible result. The methods merely determine genotypes for future use and assigning to a group, but the future use is not result of the methods as claimed. Determining could be directed merely to looking at a database file on a computer or a patient chart.

The claim 28 is drawn to methods of predicting the level of care required, by determining the genotype of both alleles of the APOE gene and assigning a patient to a predicted level of care group based on the genotype. The methods as claimed, do not

produce any physical transformation or produce a tangible result. The claims as written, encompass mere mental steps i.e. determining a genotype and assigning to a group. The steps of determining the genotype of two copies of APOE gene, does not produce any physical transformation or produce a tangible result. The methods merely determine genotypes and assign to groups for future use, but the future use is not result of the methods as claimed. Determining could be directed merely to looking at a database file on a computer or a patient chart.

The courts have stated that "While a scientific truth, or the mathematical expression of it, is not patentable invention, a novel and useful structure created with the aid of knowledge of scientific truth may be."; Warmerdam, 33 F.3d at 1360, 31 USPQ2d at 1759 ("steps of locating' a medial axis, and creating' a bubble hierarchy . . . describe nothing more than the manipulation of basic mathematical constructs, the paradigmatic abstract idea'") (see MPEM § 2106 IV).

The courts have stated that manipulation of abstract concepts or ideas constitute non-statutory subject matter.

> If the "acts" of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the acts are not being applied to appropriate subject matter. Schrader, 22 F.3d at 294-95, 30 USPQ2d at 1458-59. Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process.
>
> In practical terms, claims define nonstatutory processes if they:
>
> - consist solely of mathematical operations without some claimed practical application

(i.e., executing a "mathematical algorithm"); or

- **simply manipulate abstract ideas**, e.g. a bid (Schrader, 22 F.3d at 293-94,30

USPQ2d at 1458-59) or a bubble hierarchy (Warmerdam, 33 F.3d at 1360, 31

USPQ2d at 1759), without some claimed practical application.

(see MPEP § 2106 IV (B) (1)).

It is further noted that In re Schrader states: "the grouping or regrouping of bids cannot constitute a physical change, effect or result".... "The only physical effect or result which is required by the claim is the entering of bids in a "record," a step that can be accomplished simply by writing the bids on a piece of paper or chalkboard. For purposes of Section 101, such activity is indistinguishable from the data gathering steps which we said in *In re Grams*, 888 F.2d 835, 12 USPQ 2d 1924 (Fed. Cir. 1989), were insufficient to impart patentability to a claimed involving the solving of a mathematical algorithm". Therefore, the courts have stated that identifying without physical manipulation, is indistinguishable from data gathering and insufficient to impart patentability. Hence, the instant claims drawn to methods of determining responsiveness, or predicting the level of care by determining the genotype of APOE are non-statutory subject matter.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

15. Claims 1-3, 6-9 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Fang et al (US PGPUB 2002/0016320 filed June 30, 2000).

The instant specification teaches, "the terms 'AD and DAT' are taken to mean the same disease state and are used interchangeably"(see page 15, 1st full paragraph).

With regards to claims 1-3 and 6, Fang et al teaches a method of treating patients with cognition problems or who may be determined to be at risk of Alzheimer's disease (AD) through the detection of APOE4 (the genotype associate with the APOE ε-4 protein) by compounds employed in the methods of the patent (see column 52, lines 45-54). Fang et al teaches agents of the method include acetylcholine esterase inhibitors such as tacrine (tetrahydroaminoacridine, marketed as COGNEX®.), donepezil hydrochloride, (marketed as Aricept®), and rivastigmine (marketed as Exelon®). Fang et al thus teaches a method to prevent deterioration of cognitive function in patients by treatment with rivastigmine.

The instant specification teaches AD results in a steadily worsening of behavioral problems that coincide with the deterioration in cognitive function.

With regards to 7, 9, Fang et al teaches the treatment of AD patients based on the APOE4 the genotype associate with the APOE ε-4 protein) by compounds employed in the methods of the patent (see column 52, lines 45-54). Fang et al teaches agents of the method include acetylcholine esterase inhibitors such as tacrine (tetrahydroaminoacridine, marketed as COGNEX®.), donepezil hydrochloride, (marketed as Aricept®), and rivastigmine (marketed as Exelon®). Thus according to the specification Fang et al teaches preventing the worsening of behavioral problems in patients.

With regards to claim 8, the specification teaches, "the terms 'AD and DAT' are taken to mean the same disease state and are used interchangeably"(see page 15, 1st full paragraph). Thus Fang et al teaches wherein the dementia is DAT.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 1-9, 11-20, and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rose et al (US Patent 5,508,167, issue April 16, 1996) in view of Rosler et al (British Medical Journal (1999) volume 318, pages 633-640).

Rose et al teaches that that the presence of the APOE4 isoform of APOE indicates the subject at risk of developing Alzheimer's disease (see column 3, lines 29-35). Rose et al teaches that the risk of AD increased by a factor of 2.84 for each additional APOE4 allele present, and patients with the APOE4/ APOE4 genotype were more than 8 times as likely to be affected (see column 23, lines 49-60).

The specification teaches, "the terms 'AD and DAT' are taken to mean the same disease state and are used interchangeably"(see page 15, 1st full paragraph).

Rose does not teach administering treatment to a patient comprising rivastigmine to prevent deterioration of cognitive function (claims 1-4). Rose does not teach treatment of a patient with rivastigmine to prevent worsening of behavior problems (claims 7-9 and 11). Rose does not teach treatment of a patient with rivastigmine to improve cognitive impairment (claims 12-17). Rose does not teach treatment of a patient with rivastigmine to improve behavioral problems in patients with dementia (claims 19-20, 22-24).

However, Rosler et al teaches a study of the efficacy of rivastigmine on patients with AD. Rosler teaches that treatment with 10.4 mg/day of rivastigmine (see page 635, column 1, 3rd full paragraph) resulted in an improved cognitive subscale score in AD patients, while patients on the placebo continued to deteriorate (see page 635, 1st column, last paragraph). Rosler further teaches the use of the ADAS-Cog score for the determination of cognitive function (see table 1). Rosler thus teach a method to prevent deterioration of cognitive function as measure by ADAS-Cog score in a patient with dementia by use of rivastigmine at a dose of 6mg/ml or higher a day (claims 1-6).

The specification teaches AD results in a steadily worsening of behavioral problems that coincide with the deterioration in cognitive function. Thus the teachings of Rosler discussed above inherently teach that the treatment with rivastigmine prevents worsening of behavior (claims 7-9 and 11). Further Rosler et al teaches that patients treated with placebo had a significant decrease in clinician interview scores (see table 3). Rosler further teaches the global assessment of behavior is assessed as a part of this score (see table 1). This global assessment of behavior inherently encompasses depression, psychosis, delusions, sleep disturbance, wandering, anger outbursts, aggression, agitation, apathy, anxiety, suspiciousness, fearfulness and paranoia.

Thus Rosler teaches that treatment with rivastigmine prevents behavior worsening.

Rosler teaches that the treatment with rivastigmine at thigh doses (10.4 mg/day) improved cognitive impairment (see page 635, 1st column, last paragraph). Rosler further teaches the high 53 of 199 patients treated with the high dose of rivastigmine had a greater than 4 point improvement on the ADAS-Cog scale (see table 3) (claims 12-18).

Rosler further teaches patients treated with high doses of rivastigmine had statistically significant increases in clinician interview based impression of change scales relative to placebo treated patients (see table 3). Further Rosler teaches that 40% of patients with the high dose rivastigmine demonstrated improvement in the clinician interview score (see table 3) ($p<0.001$). Thus Rosler et al teaches the

treatment of patients with AD by administration of greater than 6mg/day of rivastigmine improves behavioral problems (claims 19-20, 22, 24).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the results of the genotyping assay taught by Rose as a method of diagnosing and prognosing dementia and AD in a patient and then treat the patient with rivastigmine as taught by Rosler. The ordinary artisan would be motivated to treat the patients identified by Rose's method as being genetically predisposed to AD with the rivastigmine of Rosler because Rosler teaches rivastigmine is one of the most successful treatments for AD. Rosler further teaches that the rivastigmine is well tolerated in the patients studied.

Summary

No claims are allowed over prior art cited.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Steven Pohnert

JEANINE A. GOLDBERG
PRIMARY EXAMINER
5/9/07